

REMARKS

Claims 16-29 and 31-44 are pending and stand rejected in the final Office action issued June 18, 2003. There are two outstanding rejections to these claims under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 103(a). These rejections are addressed below.

Rejection of Claims for Alleged Indefiniteness

Claims 16-29 and 31-44 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed. As shown in the amendment filed January 2, 2003, the meaning of “indirect causes” is clearly understood by the person of ordinary skill in the art. For example, the specification clearly distinguished indirect causes from direct causes by providing examples of indirect causes on page 31, line 31 to page 32, line 5: “The indirect causes are classified into the sepsis syndrome severe non-thoracic trauma, hypertransfusion during emergency resuscitation, and an artificial cardiac pulmonary bypass surgery.” These show by example types of indirect conditions that lead to hypoxemia in acute lung injury, and thereby clearly depict the meaning of indirect causes. Thus, the specification clearly shows multiple examples of indirect causes were known to persons of ordinary skill in the art and therefore the meets and bounds of the claims were clearly delineated.

The Office alleged in the action dated June 18, 2003 that limitations from the specification cannot be read into the claims and there are many indirect causes which may or may not be intended within the meets and bounds of the claimed subject matter. The applicability of this position is not understood. Specifically, the portions of this specification noted in the amendment filed January 2, 2003 and this response are featured to show that the person of ordinary skill in the art understood the meets and bounds of the term “indirect causes” and were not featured to read limitations into the claims. Thus, the listing of multiple indirect causes that lead to hypoxemia in acute lung injury are indicative that the person of ordinary skill in the art understood the meets and bounds of the term.

In the Advisory Action dated January 29, 2004, the Office stated that the rejection of claims 19-22 and 34-37 for alleged indefiniteness had been overcome, but the rejection was maintained for other claims having the general term “indirect causes.” Because the indirect causes of acute lung injury specified in claims 19-22 are acceptable to the Office as being definite, the broader term also should be acceptable as these examples are representative of the scope and meaning of the broader term. Therefore, the scope and meaning of the term is definite. Accordingly, it is respectfully requested that the Office withdraw the rejection of claims 16-29 and 31-44 for alleged indefiniteness under 35 U.S.C. § 112, second paragraph.

Rejection of Claims for Alleged Obviousness

Claims 16-29 and 31-44 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Folkesson *et al.* in view of Slotman. The Office cites Slotman for the alleged teaching that IL-8 was known as an inflammatory mediator of hypoxemia in acute lung injury resulting from indirect causes. The Office cites Folkesson for the alleged teaching that IL-8 was critical for the development of lung injury and that neutralization of IL-8 provided a therapeutic treatment for acute lung injury. The rejection is respectfully traversed. The cited combination does not teach or suggest that IL-8 should be targeted for treating hypoxemia in acute lung injury resulting from indirect causes, and provides no reasonable expectation of success for doing so.

As summarized above, the Office is of the view that the Slotman document suggests the use of an anti-IL-8 antibody for treatment of lung injury, and therefore the present claims are not inventive over the document. However, Ivey, C.L. *et al.*, *J. Clin. Invest.* 2720-2728 (1995) (included with the concurrently filed supplemental information disclosure statement) shows that IL-8 is produced by myocardial ischemic reperfusion injury. In addition, Lefer, A.M. *et al.*, *Br. J. Pharmacol.* (1991), 103, 1153-1159 (included with the concurrently filed supplemental information disclosure statement) shows administration of IL-8 prevents myocardial infarction. According to Lefer *et al.*, it is shown that an increase in IL-8 blood levels is effective to prevent myocardial infarction. Therefore, a person of ordinary skill in the art would have considered an anti-IL-8

antibody, which may neutralize the IL-8, would worsen a myocardial infarction. Hence, the fact that IL-8 is detected in a disease does not mean that an anti-IL-8 antibody is effective for treatment and prevention of the disease. Accordingly, Slotman does not teach or suggest methods of treating acute lung injury by targeting IL-8 with an antibody.

As summarized above, the Office is of the view that Folkesson teaches an anti-IL-8 antibody is useful for treatment of lung injury, and therefore, the combination of the cited Slotman and Folkesson documents suggests treating hypoxemia using an anti-IL-8 antibody. This is not the case as Folkesson fails to remedy the defects of Slotman.

First, Folkesson reports only the effects of an anti-IL-8 antibody on direct injury of the lung caused by acid aspiration. It appears that the Office does not distinguish direct injury and indirect injury. In this connection, according to the Conference Report of the American-European Consensus Conference on ARDS (Bernard G.R. *et al.*, *Am. J. Respir. Crit. Care Med.*, 149, p. 818-824, (1994), included with the concurrently filed supplementary information disclosure statement), Adult Respiratory Distress Syndrome (ARDS) and Acute Lung Injury (ALI) are categorized as direct injury and indirect injury, respectively (p. 821, the left column, bottom to the right column top). The direct injury and indirect injury are caused by completely different mechanisms, and therefore, a substance which is effective to treat a direct injury is not necessarily effective to treat an indirect injury.

Second, the divergent effect of lidocaine on treatment of direct injury and indirect injury is evidence that direct lung injury is a condition distinct from indirect injury. Nishina *et al.*, Acid Aspiration (*Anesthesiology*, 88, 1300-1309, Abstract) shows that the administration of lidocaine after 10 minutes and before 10 minutes of hydrochloric acid inhalation was effective. On the other hand, for treatment of indirect injury by endotoxin infusion (*Anesthesiology*, 83, 169-177, (1995), Abstract), administration of lidocaine just after endotoxin infusion did not provide a significant effect. According to Mikawa K. *et al.*, *Anesthesiology*, 81, 689-699 (1994), administration of lidocaine just before indirect injury by endotoxin infusion was effective. These documents are included with the concurrently filed supplementary information disclosure statement. As can be

seen from this evidence, a substance effective for treatment of a direct injury is not necessarily effective for treatment of an indirect injury. Thus, there was no reasonable expectation that indirect injury could be treated successfully by administering an anti-IL-8 antibody in view of the combination of Folkesson and Slotman since neither document addressed treatment of indirect lung injuries. Because there was no reasonable expectation for successfully treating an indirect lung injury using an anti-IL-8 antibody, it was not obvious to try this therapeutic approach.

Another deficiency of the cited combination was addressed in the response to final Office action filed December 13, 2003 and reiterated here. Slotman disclosed no treatment methods and provided no teaching or suggestion as to which cell mediators lead to the inflammatory conditions discussed therein. While Slotman mentioned IL-8 in a list of more than seventeen (17) potential causative of agents of certain systemic inflammatory conditions, the disclosure does not teach or suggest IL-8 alone as a target for treating hypoxemia in acute lung injury resulting by indirect causes. Specifically, there is nothing in Slotman or Folkesson suggesting that one skilled in the art should specifically target IL-8 for the treatment of hypoxemia in lung injury resulting from indirect causes and not the other potential causative agents listed in Slotman. There is nothing in the Slotman disclosure that teaches or suggest one of ordinary skill in the art would pick IL-8 out of the long list of other molecules that allegedly cause inflammatory conditions. And as noted previously, Folkesson does not provide the motivation to choose IL-8 from the list because it is limited to treating lung injury resulting from direct causes, which is a distinct condition from lung injury resulting from indirect causes. Thus, a person of ordinary skill in the art would not have chosen IL-8 as a causative agent of hypoxemia from the combination of Slotman and Folkesson, and therefore the claimed methods are not *prima facie* obvious.

CONCLUSIONS

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or fees due in connection with this document to **Deposit Account No. 03-1952** referencing docket no. 350292000500 However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 15, 2004

Respectfully submitted,

By 

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Atty Docket No.: 350292000500

Inventor: Kouji MATSUSHIMA, et al.

Application No.: 09/202,791

Filing Date: December 22, 1998

Title: THERAPEUTIC AGENT FOR ACUTE LUNG INJURY RESULTING FROM
INDIRECT CAUSES COMPRISING ANTI-IL-8 ANTIBODY AS ACTIVE
INGREDIENT

Documents Filed:

Transmittal (1 page)

Fee Transmittal (1 page, in duplicate)

Petition for Extension of Time Under 37 CFR 1.136(a) (1 page)

Notice of Appeal (1 page)

Amendment After Final Action (37 C.F.R. Section 1.116) (9 pages)

Attachment to Amendment: Review of Medical Physiology (11 pages)



DEC 29 2003

MORRISON & FOERSTER
SAN DIEGO

Via: First Class Mail

Sender's Initials: BDG3/jab15

Date: December 18, 2003



PTO/SB/31 (05-03)
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NOTICE OF APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES		Docket Number (optional) 350292000500	
In re Application of Kouji MATSUSHIMA, et al.			
Application Number 09/202,791		Filed December 22, 1998	
For THERAPEUTIC AGENT FOR ACUTE LUNG INJURY RESULTING FROM INDIRECT CAUSES COMPRISING ANTI-IL-8 ANTIBODY AS ACTIVE INGREDIENT			
Art Unit 1651		Examiner D. Ware	

Applicant hereby **appeals** to the Board of Patent Appeals and Interferences from the last decision of the examiner.

The fee for this Notice of Appeal is (37 CFR 1.17(b))

\$ 330.00

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by half, and the resulting fee is:

\$

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☒ The Director has already been authorized to charge fees in this application to a Deposit Account. I have enclosed a duplicate copy of this sheet.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 03-1952. I have enclosed a duplicate copy of this sheet. Fee Transmittal form (PTO/SB/17) is attached to this submission in duplicate.

☐ A petition for an extension of time under 37 CFR 1.136(a) (PTO/SB/22) is enclosed.

I am the

☐ applicant /inventor

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

☐ attorney or agent of record.

☒ attorney or agent acting under 37 CFR 1.34(a).

Registration number if acting under 37 CFR 1.34(a). 47,608

Signature

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Telephone Number

December 18, 2003

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of 1 forms are submitted.

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: MS AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: 12/18/03

Signature: Judy Bridgwater

(Judy Bridgwater)